REMARKS

Entry of the foregoing and further and favorable consideration of the subject application are respectfully requested and such action is earnestly solicited.

As correctly stated in the Official Action, Claims 1-18, 20, 21, and 23-29 are currently pending. Claims 11-17, 20, 23-25, and 27-29 stand withdrawn from consideration. Claims 1-10, 18, 21, and 26 stand rejected.

By the present amendment, an Abstract on a separate sheet, modeled on the abstract of the priority document WO 00/24896 is submitted herewith. Claim 18 has been canceled, without prejudice to or disclaimer of the subject matter contained therein. Applicants expressly reserve the right to file a continuation or divisional application on any subject matter canceled by the present amendment. Claims 1, 6-8, and 21 have been amended. Support for the amendment to claim 1 can be found on, at least, page 8 of the specification. New claim 30 has been added. Support for new claim 30 can be found in claim 13, as originally filed. No new matter has been added.

Objections to the Drawings

The draftsperson has objected to the quality of the Drawings. New formal drawings are submitted herewith. Withdrawal of this objection is respectfully requested.

Objections to the Specification

The specification stands objected to as lacking an Abstract of the Disclosure as required by 37 C.F.R. § 1.72(b). By the present amendment, an Abstract is submitted herewith on a separate sheet. Withdrawal of this objection is respectfully requested.

Claim Objections

Claim 1 stands objected to as encompassing more than one invention. The Examiner asserts that claim 1 should be amended to read only upon the elected invention. By the present amendment, claim 1 has been amended to read only upon the elected invention. Withdrawal of this objection is respectfully requested.

Claim 6 stands objected to as unclear in the meaning of the word "or" in line 2. Claim 6 has been amended to delete the recitation of "or" in line 2. Withdrawal of this objection is respectfully requested.

Claim 21 stands objected to for lacking an article at the beginning of the claim. Claim 21 has been amended to include "The" at the beginning of the claim. Withdrawal of this objection is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-10, 18, 21, and 26 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. Specifically, the Examiner appears to object to the

recitation of "elements" in claim 1 and "at least one DNA sequence which ensures...." in claim 18. By the present amendment, claim 18 has been canceled, thereby mooting this rejection as it applies to this claim. Without conceding to the merits of this rejection and solely in an effort to expedite prosecution, claim 1 has been amended to recite a "promoter and/or regulatory sequence," rather than an "element." Exemplary promoters and regulatory sequences that can be used to drive expression in a target cells are discussed in detail on page 8 of the present specification. Moreover, one skilled in the art can readily select other promoters and regulatory sequences already known in the art to drive expression. Accordingly, Applicants respectfully submit that the present application contains adequate written description of the presently claimed invention. Finally, Applicants note that the U.S. Patent and Trademark Office database of patents contains numerous patents where promoter and/or regulatory sequences are recited in claims without specific sequence data. *See, e.g.*, claim 11 of U.S.P.N. 6,570,064. Applicants respectfully submit that specific sequence information is not required to satisfy the written description requirement. Moreover, as numerous and diverse sequences can be used as promoters and/or regulatory sequences, recitation of specific sequence information is impractical. Withdrawal of this rejection is respectfully requested.

Claims 1-10, 18, 21, and 26 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled. The Examiner argues that the claims encompasses any gene therapy or vaccine composition. Particularly, the Examiner asserts that the specification does not disclose how to practice the *in vivo* aspect of the invention, such as the delivery of

the vectors so that they reach significant numbers of target cells selectively and evidence that a therapeutic effect *in vivo*. The Examiner points to the unpredictability of gene therapy as evidence that the presently claimed invention is not enabled. Claim 18 has been canceled by the present amendment, thereby mooting this rejection as it applies to this claim. This rejection, to the extent that it applies to the remaining claims as amended, is respectfully traversed.

By the present amendment, independent claim 1 has been amended to recite "at least one nucleic acid sequence containing at least one gene of therapeutic interest...[that] encodes all or part of an antibody...capable of binding to a polypeptide which is selected from the group consisting of all or part of the TCR complex."

Applicants respectfully submit that the present specification describes nucleic acids and vectors which encode all or part of an antibody able to bind to a cytotoxic effector cell or to a helper T lymphocyte. Examples of such vectors are disclosed in Example 2, which teaches the construction of MVA vectors comprising a nucleic acid coding part of an anti-CD3 or an anti-TCRα/β antibody. The functionality of such vectors, for the treatment of cancer, is illustrated in Examples 2-4, which show that tumor cells infected with the vectors according to an embodiment of the invention, are more vulnerable, *in vitro*, to the cells of the immune system.

Applicants respectfully submit that it would not have required undue experimentation to practice the presently claimed invention *in vivo*. Applicants submit herewith as Exhibit A a publication by S. Paul et al. (*Cancer Gene Therapy*, 9:470-477 (2002)). Paul et al. disclose experimental results obtained, *in vivo*, in mice using the MVA

vectors (MVAN-KT3, MVA-H57) described in the working examples of the present specification. Paul et al. injected the vectors, via the intratumoral route (as disclosed in the specification on page 14, 2nd paragraph) into mice bearing tumors (see page 472, 2nd column, 2nd full paragraph of Paul et al.). The results disclosed in Figure 4 (page 474) and Table 1 (page 475) of Paul et al. indicate that the treated animals have increased survival times compared to mice injected with a control vector (see page 475, lines 3 to 6). Moreover, some of the surviving mice are also resistant to a second injection of tumor cells.

Paul et al. demonstrates, that contrary to the Examiner's position, the vectors according to the presently claimed invention are able to transduce an efficient amount of tumor cells and have a measurable therapeutic effect *in vivo*. Applicants respectfully submit that the Paul et al. publication provides evidence that the presently claimed invention can be used *in vivo* according to the intended use.

Applicants further point out that Paul et al. also rebut the Examiner's comments regarding expression in selected target cells because intratumoral injection, for example, is shown to be an effective technique of administration. The use of localized delivery of the biological material of the presently claimed invention would allow one skilled in the art to control the cells that are transfected.

Applicants submit that the presently claimed invention is enabled. Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-10, 18, 21, and 26 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

Claim 1 stands rejected for the recitation of "elements which ensure the expression of said gene in vivo in target cells." Without conceding to the merits of this rejection and solely in an effort to expedite prosecution, claim 1 has been amended to recite "a promoter and/or regulatory sequence" instead of elements. Such promoters and regulatory sequences are exemplified on page 8 of the specification. Applicants are unclear as to the rejection of claim 1 for the recitation of "at least one DNA sequence which ensures the expression of a compound which is involved in the activation of cytotoxic effector cells or helper T lymphocytes" (see page 12 of the Official Action) as this phrase does not appear in claim 1, but rather claim 18. Withdrawal of this rejection is respectfully requested.

Claim 6 stands rejected for the recitation of "said vector comprises at least one said nucleic acid sequence" and "said vector comprises at least one nucleic acid complexed with a substance of a polymer group." Without conceding to the merits of this rejection and solely in an effort to expedite prosecution, claim 6 has been amended to recite "wherein said vector is complexed with a substance" of a polymer group. Withdrawal of this rejection is respectfully requested.

Claims 1, 7, and 8 stand rejected for containing multiple phrases which are allegedly not clear in their interrelation. Without conceding to the merits of this rejection and solely in an effort to expedite prosecution, claims 1, 7, and 8 have been amended to

delete, *inter alia*, the recitations of "such a cell" and "T lymphocyte." Withdrawal of this rejection is respectfully requested.

Claim 18 stands rejected as indefinite. By the present amendment, claim 18 has been canceled, thereby mooting this rejection.

Rejections Under 35 U.S.C. § 102

Claims 1-4, 6-10, 18, 21, and 26 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Schneck et al. (U.S. Patent No. 6,448,071). The Examiner argues that Schneck et al. disclose a nucleic acid sequence encoding MHC class II or TCR heterodimers and murine antibody heavy and light chains in a baculovirus expression system, wherein the expressed fusion product has high affinity to CTL. Claim 18 has been canceled by the present amendment, thereby mooting this rejection as it applies to this claim. This rejection, to the extent that it applies to the remaining claims as amended, is respectfully traversed.

To anticipate a claim under 35 U.S.C. § 102, a reference must disclose or suggest each and every element of the presently claimed invention. By the present amendment, independent claim 1 has been amended to recite that the antibody to be expressed "is capable of binding to a polypeptide selected from the group consisting of all or part of the TCR complex."

Schneck et al. do not disclose nucleic acid sequences encoding all or part of an antibody that is capable of binding to a polypeptide of all or part of the TCR complex. Rather, Schneck et al. disclose vectors containing the sequence of MHC class II or TCR

heterodimers. An antibody that recognizes the TCR complex is not produced in Schneck et al., but rather an antibody/TCR heterodimer fusion protein is produced. Accordingly, Schneck et al. do not disclose each and every element of the presently claimed invention and, therefore, cannot be anticipatory. Withdrawal of this rejection is respectfully requested.

Claims 1-6, 18, 21, and 26 stand rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Wang et al. (U.S. Patent No. 6,132,980). The Examiner argues that Wang et al. disclose "a nucleic acid construct encoding a therapeutic gene of interest, i.e., a tumor antigen that could be recognized by CTL." Claim 18 has been canceled by the present amendment, thereby mooting this rejection as it applies to this claim. This rejection, to the extent that it may apply to the remaining claims, as amended, is respectfully traversed.

By the present amendment, independent claim 1 has been amended to recite that the antibody to be expressed "is capable of binding to a polypeptide selected from the group consisting of all or part of the TCR complex."

Applicants respectfully submit that the Wang et al. publication does not disclose nucleic acid constructs that encode "all or part of an antibody that is capable of binding to all or part of the TCR complex." As the Examiner admits, Wang et al. disclose nucleic acids that encode an antigen, not an antibody that recognizes a polypeptide consisting of all or part of the TCR complex. Accordingly, Wang et al. does not disclose each and every

element of the presently claimed invention and, therefore, cannot be anticipatory. Withdrawal of this rejection is respectfully requested.

Conclusions

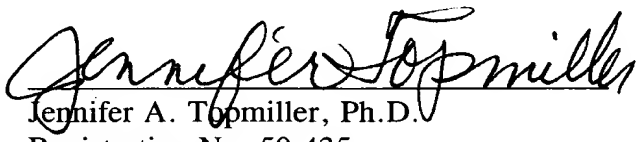
From the foregoing, further and favorable consideration in the form of a Notice of Allowance are respectfully requested and such action is earnestly solicited.

If there are any questions concerning this amendment or the application in general, the Examiner is requested to telephone Applicants' undersigned representative so that prosecution may be expedited.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: June 3, 2003

By: 
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Attachment to Amendment dated June 3, 2003

Mark-up of Abstract

The invention concerns a biological material for preparing pharmaceutical compositions for treating mammals[, comprising:] including either a nucleic acid sequence containing at least a gene of therapeutic interest and elements expressing said gene *in vivo* in target cells genetically modified by one [said] such nucleic sequence; or at least a target cell not producing antibodies naturally, genetically modified *in vitro* by at least one [said] such nucleic acid sequence. [The invention is characterized in that said] The gene of therapeutic interest codes for all or part of an antibody expressed at the surface of said target cell and [said] such an antibody is capable of fixing itself to a polypeptide present at the surface of a cytotoxic effector cell or a T lymphocyte helper and involved in the process activating such a cell.

Attachment to Amendment dated June 3, 2003

Mark-up of Claims 1, 6-8, and 21

1. (Twice Amended) A biological material for treating mammals, comprising:

[- either] at least one nucleic acid sequence containing at least one gene of therapeutic interest and [elements] a promoter and/or regulatory sequence which [ensure] ensures the expression of said gene in vivo in target cells intended to be genetically modified with said nucleic acid sequence;

[- or at least one target cell which does not naturally produce antibodies and which is genetically modified *in vitro* with at least one nucleic acid sequence above,] wherein said gene of therapeutic interest encodes all or part of an antibody which will be expressed at the surface of said target cell, wherein said antibody is capable of binding to a polypeptide which is [present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell] selected from the group consisting of all of part of the T-Cell Receptor (TCR) complex.

6. (Twice Amended) The biological material according to claim 3, wherein said vector [comprises at least one said nucleic acid sequence] is complexed with [or] a substance selected from the group consisting of a cationic amphiphile, a cationic or neutral polymer, a protic polar compound, and an aprotic polar compound, or their derivatives.

7. (Twice Amended) The biological material according to claim 1, when said nucleic acid sequence comprises a gene encoding the heavy chain of an antibody [capable

Attachment to Amendment dated June 3, 2003

of binding to a polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell,] fused with a transmembrane polypeptide.

8. (Twice Amended) The biological material according to claim 7, wherein said nucleic acid sequence further contains a gene encoding the light chain of an antibody [capable of binding to a polypeptide which is present at the surface of a cytotoxic effector cell or of a helper T lymphocyte, and which is involved in the process of activation of such a cell].

21. (Twice Amended) [Pharmaceutical] The pharmaceutical composition comprising a biological material according to claim 1, advantageously in combination with a pharmaceutically acceptable vehicle.

ABSTRACT

The invention concerns a biological material for preparing pharmaceutical compositions for treating mammals including either a nucleic acid sequence containing at least a gene of therapeutic interest and elements expressing said gene *in vivo* in target cells genetically modified by one such nucleic sequence; or at least a target cell not producing antibodies naturally, genetically modified *in vitro* by at least one such nucleic acid sequence. The gene of therapeutic interest codes for all or part of an antibody expressed at the surface of said target cell and such an antibody is capable of fixing itself to a polypeptide present at the surface of a cytotoxic effector cell or a T lymphocyte helper and involved in the process activating such a cell.